UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF VIRGINIA

WHOLE WOMAN'S HEALTH ALLIANCE, *et al.*, Plaintiffs, v. UNITED STATES FOOD AND DRUG ADMINISTRATION, *et al.*, Defendants.	Case No. 3:23-cv-00019-RSB

DEFENDANTS' COMBINED MEMORANDUM IN SUPPORT OF CROSS-MOTION FOR SUMMARY JUDGMENT AND IN OPPOSITION TO PLAINTIFFS' MOTION FOR SUMMARY JUDGMENT

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INTRODUCTION

In 2000, the U.S. Food and Drug Administration approved mifepristone as safe and effective for medical termination of early pregnancy subject to certain restrictions to assure safe use.[1] Since 2008, those restrictions have been called "elements to assure safe use" (ETASU) and are part of a Risk Evaluation and Mitigation Strategy (REMS). Among other things, the restrictions on mifepristone have always required that prescribers certify that they meet certain criteria and that patients sign a Patient Agreement Form disclosing risks of the drug. Until 2023, the restrictions also included a requirement—known as the "in-person dispensing requirement"—that mifepristone be dispensed only in certain healthcare settings by or under the supervision of a certified prescriber.

In 2021, FDA directed the sponsors of mifepristone to submit a proposed modification to the REMS to eliminate the in-person dispensing requirement and add a pharmacy certification requirement. That directive followed FDA's comprehensive review of adverse event reports, literature, and other information available since an earlier modification in 2016. FDA approved the modified REMS on January 3, 2023. As a result, mifepristone may be dispensed in-person or by mail and must be dispensed by or under the supervision of a certified prescriber or by a certified pharmacy. In short, FDA made mifepristone's REMS less burdensome in response to evidence that an

[1] This brief uses "mifepristone" to refer to drug products approved for medical termination of early pregnancy. FDA has also approved another manufacturer's drug, Korlym, which has mifepristone as its active ingredient and is approved for the treatment of Cushing's syndrome. This litigation does not affect Korlym.

existing restriction (the in-person dispensing requirement) was no longer needed if pharmacy certification was added and the other REMS requirements were followed.

Indeed, the effect of the January 2023 REMS modification was to make mifepristone's REMS (including the ETASU) less burdensome than ever before. Yet in their Complaint, Plaintiffs—six healthcare-provider entities and one certified prescriber of mifepristone—challenge the January 2023 REMS modification as unjustified. They allege that mifepristone is safe without a REMS, even though FDA—the expert agency charged with reviewing drug safety—has not reached that conclusion. From there, Plaintiffs argue that FDA should have eliminated the REMS entirely, rather than approve modifications to the REMS that had the effect of making it less burdensome. The Court should reject these arguments, deny Plaintiffs' motion for summary judgment, and grant summary judgment to Defendants.

First, Plaintiffs lack Article III standing. Plaintiffs allege that the REMS burdens patients and other unidentified healthcare providers. This theory cannot establish standing because Article III requires Plaintiffs to show that *they* have been injured, which they fail to do. Moreover, they rely on speculative and attenuated theories of standing, similar to those the Supreme Court rejected in *FDA v. Alliance for Hippocratic Medicine*, 602 U.S. 367 (2024). Plaintiffs do not claim to be directly harmed by any REMS requirement. Instead, they claim to be indirectly harmed based on speculation about how the REMS influences third parties not before the Court.

Second, Plaintiffs failed to administratively exhaust their claims by filing a citizen petition. Doing so would have given the agency an opportunity to apply its expertise in

the first instance. Neither FDA's 2020 response to a letter submitted by several States, nor the agency's 2021 REMS review, nor its response to a 2022 citizen petition demonstrates that exhaustion would be futile.

Third, Plaintiffs' APA claims fail on the merits. FDA may not approve a modification to a REMS unless the agency determines that, with the change, the drug's benefits outweigh its risks. Here, applying that standard, FDA determined that there was insufficient evidence to eliminate the REMS entirely. Plaintiffs disagree, faulting FDA for supposedly failing to consider relevant statutory factors. But each statutory factor that Plaintiffs identify either was considered by FDA or was not relevant to the modification decision.

Nor do Plaintiffs' attacks on FDA's consideration of the evidence or the agency's reasoning have merit. FDA considered all evidence before it relevant to whether the elements of the Mifepristone REMS Program are necessary to maintain a favorable benefit/risk (safety) profile for mifepristone. FDA found insufficient evidence to demonstrate that mifepristone would continue to have a favorable safety profile if the prescriber certification requirement or Patient Agreement Form were eliminated. But FDA found that there was sufficient evidence supporting removal of the in-person dispensing requirement, provided that all other REMS requirements were met and a pharmacy certification requirement was added.

Finally, Plaintiffs' equal protection claims also fail. Those claims are subject to rational basis review. FDA's determination that the REMS is necessary to assure safe use of mifepristone supplies that rational basis.

BACKGROUND

I. Statutory and Regulatory Background

The Federal Food, Drug, and Cosmetic Act (FDCA) generally prohibits the interstate distribution of new drugs that have not received FDA approval. 21 U.S.C. §§ 331(d), 355(a). FDA approves a new drug application if the drug is shown to be safe and effective for its intended use. *Id.* § 355(d); *see also* 21 C.F.R. §§ 314.50, 314.105(c). Similarly, when a drug's sponsor proposes changes to the drug's conditions of approval (such as changes to labeling or to restrictions relating to its distribution or use), FDA reviews the scientific evidence submitted in support of the proposal to determine whether it should be approved. *See* 21 C.F.R. § 314.70. And in determining whether a drug is "safe," FDA examines whether the benefits of the drug outweigh the risks. *See* FDA Guidance for Industry, *Benefit-Risk Assessment for New Drug and Biological Products* (Oct. 2023) ("Because all drugs can have adverse effects, the demonstration of safety requires a showing that the benefits of the drug outweigh its risks.").[2]

In 1992, FDA promulgated regulations (the Subpart H regulations) providing for the imposition of conditions "needed to assure safe use" of certain new drugs that satisfy the other requirements for approval under the FDCA. Final Rule, 57 Fed. Reg. 58,942, 58,958 (Dec. 11, 1992) (codified at 21 C.F.R. § 314.520). In the Food and Drug Administration Amendments Act of 2007 (FDAAA), Congress codified and expanded the Subpart H regulations by giving FDA authority to require a REMS when it

[2] Available at https://www.fda.gov/media/152544/download.

determines that restrictions are necessary to ensure that the benefits of a drug outweigh the risks. *See* Pub. L. No. 110-85, tit. IX, § 901 (codified at, *inter alia*, 21 U.S.C. § 355-1). FDA may require that a REMS include ETASU if necessary to mitigate a serious health risk and if certain statutory criteria relating to ensuring safety and minimizing the burden of restrictions are satisfied. 21 U.S.C. § 355-1(f). ETASU may include requirements that a drug's prescribers have particular training or are specially certified, that a drug be dispensed only in certain settings or by certified pharmacies, and that the drug be dispensed to patients only with evidence or other documentation of safe-use conditions. *See* 21 U.S.C. § 355-1(f)(3).

FDAAA expressly incorporated drugs with existing Subpart H restrictions to assure safe use into the new REMS framework. *See* Pub. L. No. 110-85, tit. IX, § 909 (21 U.S.C. § 331 note). Specifically, Congress "deemed" such drugs to have a REMS in effect, with the Subpart H restrictions serving as ETASU. *Id.* § 909(b). Thereafter, sponsors for such drugs were required to submit supplemental new drug applications with a proposed REMS, which FDA then reviewed. *See id.*

FDAAA also provided standards for modifying an existing REMS. *See* 21 U.S.C. § 355-1(g)(4). As relevant here, FDA may require a sponsor to "submit a proposed modification" to a REMS if the agency "determines that 1 or more goals or elements should be added, modified, or removed" from the approved REMS to "ensure the benefits of the drug outweigh the risks of the drug" or "minimize the burden on the health care delivery system of complying with the strategy." *Id.* § 355-1(g)(4)(B).

II. Factual and Procedural Background[3]

In 2000, FDA approved mifepristone (under the brand name Mifeprex) in a regimen with misoprostol for medical termination of intrauterine pregnancy through 49 days gestation. 2021 REMS 001566; FDA 0003-5; FDA 0009. At the same time, to assure mifepristone's safe use, FDA placed restrictions under Subpart H on the distribution and use of the drug product. 2021 REMS 001566; FDA 0003-5. These included requirements that (1) prescribers certify that (among other things) they have the ability to accurately date pregnancies and diagnose ectopic pregnancies, and will either provide surgical intervention if necessary or arrange for others to provide it; (2) the drug be dispensed only in certain healthcare settings, by or under the supervision of a specially certified prescriber (the in-person dispensing requirement); and (3) patients sign a Patient Agreement Form. 2021 REMS 001566; FDA 0004. FDA concluded based on a review of clinical trials and other scientific evidence that, under those conditions, mifepristone was safe and effective, in a regimen with misoprostol, to terminate an early pregnancy. 2021 REMS 001566; FDA 0003.

Because these restrictions under Subpart H were in place when FDAAA took effect, Mifeprex was "deemed to have in effect an approved [REMS]" that continued these restrictions as "elements to assure safe use." Pub. L. No. 110-85, § 909(b)(1); *see also*

[3] Although there are not disputed issues of material fact in an Administrative Procedure Act (APA) case, *see infra* p. 9, this section is intended to comply with Local Rule 56, which requires "[a]ny motion for summary judgment or any other dispositive motion" to "contain a separately captioned section setting forth with specificity the material facts claimed to be undisputed together with specific record citations in support thereof."

2021 REMS 001566; FDA 1281. In 2011, in response to a supplemental application submitted by the sponsor, FDA approved the Mifeprex REMS after determining that certain restrictions remained necessary to ensure the benefits of mifepristone outweigh the risks. FDA 1281; 2021 REMS 001565, 1566. In 2016, FDA approved a supplemental application from the sponsor proposing modifications to the conditions of approval (including the REMS) for Mifeprex, to lower the dose of mifepristone, increase the gestational age limit from 49 to 70 days, reduce the number of required in-person clinic visits from three to one, remove the requirement that mifepristone be taken at a clinic, and to allow mifepristone to be prescribed by non-physician healthcare providers licensed under state law to prescribe drugs. 2021 REMS 001565; FDA 0371-381. When FDA approved a generic version of the drug in 2019, it approved a single, shared system REMS, known as the Mifepristone REMS Program, for both Mifeprex and the generic version. 2021 REMS 001565.

FDA has since reviewed and approved modifications to the Mifepristone REMS Program that are consistent with decades of experience reflecting that, with the REMS in effect, the benefits of mifepristone outweigh the risks. As relevant here, on May 7, 2021, FDA announced that it would review the elements of the Mifepristone REMS Program to determine whether those elements should be modified. 2021 REMS 001565, 1568; 2021 REMS 000643-650. FDA's review encompassed "multiple different sources of information," including "published literature," "safety information," adverse event reports, a "REMS assessment report" submitted by the sponsors, and "information provided by advocacy groups, individuals, and the [sponsors]." 2021 REMS 001570. The

time period for the agency's literature search was March 29, 2016 (the date of the 2016 REMS modification) to July 26, 2021, and the search included publications found on PubMed and Embase as well as those provided by "advocacy groups, individuals, plaintiffs in [*Chelius v. Becerra*, No. 1:17-493-JAO-RT (D. Haw.)]," the sponsors, and "healthcare providers and researchers." 2021 REMS 001570.

On December 16, 2021, FDA announced its conclusion that "mifepristone will remain safe and effective for medical abortion if the in-person dispensing requirement is removed, provided all the other requirements of the REMS are met, and pharmacy certification is added." 2021 REMS 001599; *see also* 2021 REMS 001601. Specifically, because FDA found insufficient evidence to demonstrate that the drug would be safe without them, FDA determined that the prescriber certification and Patient Agreement Form requirements continued to be necessary components of the REMS to mitigate risks related to heavy bleeding, missed ectopic pregnancy, and other issues. 2021 REMS 001572-1578, 1596-1597.

At the same time, FDA determined that the REMS "must be modified" to remove the requirement that mifepristone be dispensed only in certain healthcare settings because this requirement is "no longer necessary to ensure that the benefits of the drug outweigh the risks." 2021 REMS 1803-1807; 1808-1811. FDA also determined that because the in-person dispensing requirement was being removed, it was necessary to add a new requirement that pharmacies that dispense the drug be certified. 2021 REMS 001600-1601. FDA reasoned that "[a]dding the pharmacy certification requirement incorporates pharmacies into the REMS, ensures that pharmacies are aware of and

agree to follow applicable REMS requirements, and ensures that mifepristone is only dispensed pursuant to prescriptions that are written by certified prescribers." 2021 REMS 001600. "[M]ifepristone will remain safe and effective" with these REMS modifications, FDA concluded, "provided all the other requirements of the REMS are met and pharmacy certification is added." 2021 REMS 001599; *see also* 2021 REMS 001601.

FDA directed the mifepristone sponsors to submit supplemental applications proposing these modifications to the REMS. 2021 REMS 001803-1807, 1808-1811. The sponsors submitted their supplemental applications on June 22, 2022, and FDA approved them on January 3, 2023. 2023 SUPP 000257-350, 351-439; 2023 SUPP 001448-1460, 1461-1465. Plaintiffs challenge that decision.

STANDARD OF REVIEW

In reviewing agency action under the APA, "the ordinary summary judgment standard under [Federal Rule of Civil Procedure 56(c)] does not apply." *Hyatt v. U.S. Patent and Trademark Office*, 146 F. Supp. 3d 771, 780 (E.D. Va. 2015). After all, "the facts are all set forth in the administrative record" and "the presence or absence of a genuine dispute of material fact is not in issue." *Id.* Instead, "summary judgment 'serves as the mechanism for deciding, as a matter of law, whether the agency action is supported by the administrative record and otherwise consistent with the APA.'" *Id.* (quoting *Sierra Club v. Mainella*, 459 F. Supp. 2d 76, 90 (D.D.C. 2006)).

That inquiry requires the Court to determine, based on the administrative record, *Camp v. Pitts*, 411 U.S. 138, 142 (1973), whether the challenged agency action was

"arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law," 5 U.S.C. § 706(2)(A), or "in excess of statutory jurisdiction, authority, or limitations," *id.* § 706(2)(C). Review under the arbitrary-and-capricious standard is "at its most deferential" with respect to an agency's scientific determinations within its area of expertise. *Balt. Gas & Elec., Co. v. Nat. Res. Def. Council, Inc.*, 462 U.S. 87, 103 (1982). "[FDA's] judgments as to what is required to ascertain the safety and efficacy of drugs fall squarely within the ambit of the FDA's expertise and merit deference from [courts]." *Schering Corp. v. FDA*, 51 F.3d 390, 399 (3d. Cir. 1995); *see also FDA v. Am. Coll. Of Obstetricians & Gynecologists*, 141 S. Ct. 578, 579 (2021) (Roberts, C.J., concurring in the grant of application stay).

ARGUMENT

I. Plaintiffs Lack Standing

To meet the "irreducible constitutional minimum of standing," *Lujan v. Defs. of Wildlife*, 504 U.S. 555, 560 (1992), Plaintiffs "must show (i) that [they] suffered an injury in fact that is concrete, particularized, and actual or imminent; (ii) that the injury was likely caused by the defendant[s]; and (iii) that the injury would likely be redressed by judicial relief," *TransUnion LLC v Ramirez*, 594 U.S. 413, 423 (2021). "The party invoking federal jurisdiction bears the burden of establishing standing—and, at the summary judgment stage, such a party can no longer rest on mere allegations, but must set forth by affidavit or other evidence specific facts." *Clapper v. Amnesty Int'l USA*, 568 U.S. 398, 411-12 (2013) (internal quotation marks and alterations omitted). Moreover, "standing is not dispensed in gross." *Lewis v. Casey*, 518 U.S. 343, 358 n.6 (1996). "Rather, a plaintiff

must demonstrate standing for each claim he seeks to press and for each form of relief that is sought." *Davis v. FEC*, 554 U.S. 724, 734 (2008) (internal quotation marks omitted).

1. Primarily, Plaintiffs rely on alleged harm *to others* to establish their Article III standing. *See, e.g.*, Compl. ¶ 107 (alleging that the "Patient Agreement Form risks the privacy of patients and providers," without mentioning Plaintiffs); *id.* ¶ 108 (alleging that privacy "is a particular concern for patients who travel from a state where abortion is banned to state where it is legal"); *id.* ¶ 109 (alleging that the Patient Agreement Form may "require[e] [patients] to make a false and potentially traumatizing attestation"); *id.* ¶ 110 (alleging that disclosure of the Patient Agreement Form to third parties would "expose providers and patients to threats of reprisal" without alleging any threats to Plaintiffs); *id.* ¶ 113 (alleging that, "for many healthcare providers" (but not naming Plaintiffs specifically), prescriber certification is burdensome); *id.* (alleging that "some providers" (but not Plaintiffs) are deterred from prescribing mifepristone by the prescriber certification requirement); *id.* ¶ 116 (alleging that the pharmacy certification requirement imposes unnecessary requirements on pharmacies); *id.* (alleging that the pharmacy certification requirement prevents patients from "decid[ing] from which pharmacy to pick up" mifepristone); Smith Decl., ECF No. 10-2, ¶ 18 (alleging that the REMS causes patients "confusion and pain"); *id.* ¶ 19 (alleging that the REMS makes "mifepristone less available for our patients"); Weems Decl., ECF No. 10-3, ¶ 13 (alleging that "before the Patient Agreement [Form] was updated in 2023, it included a statement that patients agreed to bring the Medication Guide to an emergency room,"

and that doing this "c[ould] expose" patients to "harassment and hostility"); *id.* ¶ 14 (alleging that the Patient Agreement Form "can continue to be confusing for patients"); *id.* ¶ 15 (alleging that pharmacy certification poses "an unnecessary roadblock for pharmacies" and prevents patients from picking up prescriptions at uncertified pharmacies).

Such allegations are insufficient. "The relevant showing for purposes of Article III standing . . . is . . . injury to the plaintiff." *Friends of the Earth, Inc. v. Laidlaw Envt'l Servs. (TOC), Inc.*, 528 U.S. 167, 181 (2000) (emphasis added). Thus, "even when [courts] have allowed litigants to assert the interest of others, the litigants themselves must still have suffered an injury in fact, thus giving them a sufficiently concrete interest in the outcome of the issue in dispute." *Hollingsworth v. Perry*, 570 U.S. 693, 708 (2013) (internal quotation marks and alteration omitted). In short, Plaintiffs cannot "shoehorn themselves into Article III standing simply by showing that their patients"—or other providers or pharmacies—"have suffered injuries or may suffer future injuries." *Alliance for Hippocratic Medicine*, 602 U.S. at 393 n.5.

2. Plaintiffs do not allege—let alone prove—*any* injuries of their own. They do not allege that they or their employees have been exposed or likely will be exposed to threats as a result of disclosure of a Patient Agreement Form or the fact that a prescriber is certified. They do not allege that the prescriber certification requirement prevents them or their employees from prescribing mifepristone or practicing medicine in any way they believe is appropriate. While they speculate that the prescriber certification requirement "restricts the number of available clinicians who might be able to be

certified prescribers at Plaintiffs' clinics," Compl. ¶ 115; *see also* Tong Decl., ECF No. 10-1, ¶ 12; Smith Decl. ¶ 19; Hagstrom-Miller Decl., ECF No. 10-4, ¶ 44, they do not allege that they are unable to adequately staff their clinics or that they have ever encountered a healthcare provider who would have worked at their clinics but for the REMS. Nor do they explain how they are injured when they must send a prescription to a certified pharmacy, rather than an uncertified pharmacy. *See* Compl. ¶ 116; Tong Decl. ¶ 11; Smith Decl. ¶ 19; Weems Decl. ¶ 15; Hagstrom-Miller Decl. ¶ 44.[4]

In any event, even assuming their generalized concerns constituted injury, Plaintiffs cannot satisfy the requirement of causation, which "is central to Article III standing." *Alliance for Hippocratic Medicine*, 602 U.S. at 383. As the Supreme Court explained in rejecting another challenge to FDA's actions with respect to mifepristone, a plaintiff cannot establish causation through "speculative links—that is, where it is not sufficiently predictable how third parties would react to government action or cause downstream injury to the plaintiffs." *Alliance for Hippocratic Medicine*, 602 U.S. at 383. Nor, explained the Court, do "attenuated links" based on "distant (even if predictable) ripple effects" suffice. *Id.*

[4] Plaintiffs also allege that they and others would suffer various injuries if the January 2023 REMS modification were reversed and prior, more burdensome restrictions were restored. *See, e.g.*, Compl. ¶¶ 99-104; Tong Decl. ¶ 27; Smith Decl. ¶¶ 28-34; Weems Decl. ¶¶ 19-36; Hagstrom-Miller Decl. ¶¶ 36-43. Plaintiffs relied on these alleged injuries in their unsuccessful effort to show irreparable harm warranting a preliminary injunction. *Whole Woman's Health Alliance v. FDA*, 2023 WL 5401885, at *7-8 (W.D. Va. Aug. 21, 2023). These alleged injuries cannot support standing because they are speculative (FDA has not suggested that it intends to make the REMS more burdensome) and are not fairly traceable to the January 2023 REMS modification—the only agency action Plaintiffs challenge.

Here, any injuries Plaintiffs suffer result from the independent actions of third parties not before the Court, rather than from any direct regulation. For example, Plaintiffs theorize that third parties (patients) might have their Patient Agreement Forms accessed by other third parties ("a patient's spouse, partner, or parent"), and that those third parties might threaten providers. Compl. ¶ 110. Similarly, Plaintiffs speculate that the REMS itself causes "stigma around abortion care," *id.* ¶ 115; *see also* Tong Decl. ¶ 12; Smith Decl. ¶ 17, which in turn influences the choices of third parties, hypothetically causing downstream harm to Plaintiffs. *See* Compl. ¶¶ 115, 118. Although no Plaintiff operates a pharmacy, Plaintiffs allege that the pharmacy certification requirement dissuades some third-party pharmacies from dispensing mifepristone, which indirectly affects Plaintiffs by requiring their patients to fill prescriptions at pharmacies that *do* dispense the drug. *Id.* ¶¶ 117-118. Such theories of causation are too unpredictable to satisfy Article III. And even if they were predictable, the asserted harm to Plaintiffs is the sort of "distant . . . ripple effect" that *Alliance for Hippocratic Medicine* rejected as a basis for standing.

3. For these reasons, Plaintiffs have not met their burden to show Article III standing to challenge any REMS requirement.[5] But if the Court found that a Plaintiff had standing to challenge a particular REMS requirement, that would not mean Plaintiffs may challenge, in gross, FDA's decision to retain the REMS. *See Davis*, 554 U.S.

[5] Defendants respectfully disagree with this Court's determination at the preliminary injunction stage that Plaintiffs have standing. *WWHA*, 2023 WL 5401885, at *5.

at 734. At most, they would have standing to challenge only those requirements that cause them a redressable actual or imminent concrete injury.

II. Plaintiffs Failed To Administratively Exhaust Their Claims

Plaintiffs also failed to administratively exhaust their claims through a citizen petition, as required by FDA regulations. *See* 21 C.F.R. §§ 10.45(b), (f), 10.25(a), 10.30; *see also* ECF No. 42, at 12 ("a plaintiff must exhaust 'to the extent required by statute or by agency rule as a prerequisite to judicial review'") (quoting *Darby v. Cisneros*, 509 U.S. 137, 153 (1993)).

Exhaustion requirements "serv[e] to 'allow an agency the opportunity to use its discretion and expertise to resolve a dispute without premature judicial intervention and to allow courts to have the benefit of an agency's talents through a fully developed administrative record.'" *Cavalier Tel., LLC v. Va. Elec. & Power Co.*, 303 F.3d 316, 322 (4th Cir. 2002) (quoting *Thetford Props. IV Ltd. v. Dep't of Hous. & Urban Dev.*, 907 F.2d 445, 448 (4th Cir. 1990)). Thus, a party challenging FDA's approval of a drug application or other marketing authorization must first file a citizen petition presenting the challenge to the agency. *See, e.g.*, *Ass'n of Am. Physician & Surgeons, Inc. v. FDA (AAPS)*, 539 F. Supp. 2d 4, 21-24 (D.D.C. 2008) (dismissing challenge to FDA approval of a drug application because plaintiffs failed to file a citizen petition) , *aff'd*, 358 F. App'x 179 (D.C. Cir. 2009); *Jensen v. Biden*, No. 4:21-cv-5119, 2021 WL 10280395 (E.D. Wash. Nov. 19, 2021) (dismissing challenge to emergency use authorization because plaintiffs failed to file a citizen petition); *Doe #1-#14 v. Austin*, 572 F. Supp. 3d 1224, 1234 (N.D. Fla. 2021) ("In their filings the plaintiffs introduce materials that the FDA did not receive for

consideration as part of the citizen petition challenging Comirnaty's licensure. Thus, the plaintiffs have not pursued an available administrative route available to force the FDA to consider the materials they submit here") (internal citation omitted).

Plaintiffs' claims turn on issues within the agency's expertise. They involve technical and factual assertions about, for example, safety comparisons of mifepristone to other drugs and alleged burdens of REMS requirements on the healthcare delivery system—including burdens that Plaintiffs allege have arisen only after FDA's 2021 REMS review. *See, e.g.*, Compl. ¶¶ 3, 9. Their claims also rely on studies that were not before the agency at the time of that determination. *See, e.g.*, Compl. ¶¶ 6, 68, 74, 75. Therefore, Plaintiffs' claims must be exhausted.

As this Court previously observed, "The Fourth Circuit requires a 'clear and positive showing of futility . . . before suspending the exhaustion requirement.'" *WWHA*, 2023 WL 5401885, at *5 (quoting *Makar v. Health Care Corp. of Mid-Atlantic (Care First)*, 872 F.2d 80, 83 (4th Cir. 1989)). Indeed, "[a]bsent a clear showing that an administrative agency has taken a hard and fast position that makes an adverse ruling a certainty, a litigant's prognostication that he is likely to fail before an agency is not a sufficient reason to excuse the lack of exhaustion." *Thetford Props. IV Ltd. v. Dep't of Hous. & Urban Dev.*, 907 F.2d 445, 450 (4th Cir. 1990). And this Court correctly noted that "[s]ome of the evidence and arguments cited by Plaintiffs have never been considered by FDA." *WWHA*, 2023 WL 5401885, at *6. The Court nevertheless concluded that Plaintiffs had met their burden to show futility. *Id.* Respectfully, Defendants disagree with that conclusion.

None of FDA's previous actions demonstrates that the futility exception applies. *First*, FDA never considered a 2020 letter from a coalition of States in connection with a REMS modification decision. That letter was submitted to a public docket for guidance regarding FDA's policy for certain REMS requirements during the COVID-19 public health emergency, *see* FDA-2020-D-1106-0061, and in any event did not contain all of Plaintiffs' present arguments or the studies on which Plaintiffs rely. *See WWHA*, 2023 WL 5401885, at *6.[6] FDA's response to that letter therefore does not demonstrate that it would have been futile for Plaintiffs to have presented their arguments to the agency during the 2021 REMS review or now through a citizen petition.

Second, FDA's conclusion in 2021 that the REMS must be modified but not eliminated likewise does not excuse Plaintiffs' failure to exhaust. Plaintiffs' challenge raises points that could not have been considered in 2021, including their arguments about post-*Dobbs* developments and a 2022 Canadian study. Indeed, if Plaintiffs are correct that it is certain that the outcome would have been the same had FDA considered these matters, then any failure to consider them would be harmless error. *See* 5 U.S.C. § 706 ("due account shall be taken of the rule of prejudicial error").

Third, the American College of Obstetricians and Gynecologists' (ACOG's) 2022 citizen petition did not relate to the agency's 2021 review of the REMS or to the January 2023 REMS modification. *See WWHA*, 2023 WL 5401885, at *6 (acknowledging that "the

[6] For clarity, Defendants note that FDA does not consider this letter to be a Citizen Petition under its regulations. *Contra WWHA*, 2023 WL 5401885, at *2, 6; *see* 21 C.F.R. §§ 10.20, 10.25, 10.30.

2022 citizen petition is not directly relevant to the current action"). Rather, it asked FDA to request that the sponsor of Mifeprex submit a supplemental new drug application proposing to (1) add miscarriage management as an approved indication and (2) eliminate or modify the REMS so that it would not be unduly burdensome for *that* use. 2022 CP 000072. FDA denied the citizen petition because it is up to the sponsor to decide whether to seek approval for a new indication. 2022 CP 000112-113.

Citing the Canadian study, that petition also urged FDA to exercise enforcement discretion with respect to the REMS requirements as they pertain to miscarriage management, while such a supplemental new drug application was being considered. 2022 CP 000087-88. FDA denied this request because the management of miscarriage is not a currently approved indication for mifepristone. It thus would be premature for FDA to consider any impact that the addition of this indication would have on the REMS, including whether the REMS is unduly burdensome for that use. 2022 CP 000113. Given this disposition of the petition, it was unnecessary for the agency to consider the Canadian study.

In short, nothing demonstrates that it would have been futile for Plaintiffs to present their claims (including about the Canadian study) to FDA. While it is not a foregone conclusion that FDA would find that the study supports the result Plaintiffs seek, it is also not certain that FDA would reject Plaintiffs' arguments.

III. Plaintiffs' APA Claims Are Meritless

A. FDA reasonably applied the REMS modification statutory factors

As explained above, FDA's decision to modify a REMS is governed by § 355-1(g)(4). That paragraph is titled "[m]odification" and, among other things, sets forth the factors that FDA considers when determining whether to require a sponsor to propose a REMS modification. FDA may require that a sponsor propose a modification to an existing REMS in a supplemental application to "ensure the benefits of [a] drug outweigh the risks of the drug" or to "minimize the burden on the health care delivery system." 21 U.S.C. § 355-1(g)(4)(B). FDA may not approve a supplemental application modifying a REMS unless the agency is satisfied that the evidence shows that the drug will remain safe with the modification. *Id.* §§ 355-1(g)(4)(B), 355(d); 21 C.F.R. §§ 314.1 (new drug application requirements apply to supplemental applications), 314.105(c) (approval contingent on meeting statutory standards for safety and effectiveness).

Here, FDA appropriately applied the § 355-1(g)(4)(B) factors to determine that the REMS must be modified in certain respects and that, as modified, the drug would remain safe, while minimizing the burden of the REMS. In reaching that determination, FDA did not reassess information it already considered in coming to its then-existing safety determination. Rather, it based that determination on its 2021 review of information generated after the 2016 REMS modification. 2021 REMS 001570-1571, 1572, 1577, 1604-1608.

Specifically, FDA carefully examined hundreds of publications to determine whether they supported modifications to the REMS that would continue to assure safe

use of the drug. 2021 REMS 001570-1571, 1572, 1577, 1604-1608. The agency also reviewed information from a wide variety of other sources, including healthcare providers, advocacy groups, and the *Purcell* (then *Chelius*) Plaintiffs. 2021 REMS 001570-1571, 1572, 1577, 1604-1608. FDA also considered safety information from time periods in which the in-person dispensing requirement was not being enforced during the COVID-19 public health emergency, including information from the sponsors and adverse event reports. 2021 REMS 001570. Additionally, in assessing whether to maintain the Patient Agreement Form, FDA considered the National Abortion Federation's 2020 Clinical Policy Guidelines for Abortion Care, as well as Practice Bulletins from ACOG and the Society of Family Planning, and data relating to an increase in new providers for this care obtained from well-conducted surveys. 2021 REMS 001572, 1577.

Based on its review, FDA found evidence sufficient to support eliminating the in-person dispensing requirement, so long as pharmacy certification was added and the other existing REMS elements were retained. 2021 REMS 001599; *see also* 2021 REMS 001601. FDA's determination with respect to each element was reasonable.

1. Prescriber certification. FDA explained that the evidence was insufficient to show that the benefits of mifepristone would continue to outweigh its risks if the prescriber certification requirement was removed. 2021 REMS 001573-1574, 1597. Specifically, the agency's literature review did not identify any studies comparing providers who met the qualifications that must be certified to with providers who did not, and thus found "no evidence to contradict [its] previous finding that prescribers'

ability to accurately date pregnancies, diagnose ectopic pregnancies, and provide surgical intervention or arrange for such care through others if needed, is necessary to mitigate the serious risks associated with" the drug. 2021 REMS 001573. In addition, by requiring prescribers to acknowledge that they "must report patient deaths associated with mifepristone to the manufacturer," the prescriber certification requirement "ensures that the manufacturer receives all reports of patient deaths and, in turn, fulfills its regulatory obligations to report those deaths to the FDA." 2021 REMS 001574. Moreover, FDA anticipated a "potential for doubling" the number of prescribers due to the agency's removal of the in-person dispensing requirement. 2021 REMS 001574; *see also* 2021 REMS 001597. In view of that potential, the agency determined that it was important to retain the prescriber certification to ensure that providers meet the necessary qualifications and adhere to the guidelines for use. 2021 REMS 001574; *see also* 2021 REMS 001597.

FDA therefore concluded that prescriber certification "continues to be a necessary component of the REMS to ensure the benefits of mifepristone for medical abortion outweigh the risks." 2021 REMS 001574; *see also* 2021 REMS 001597. At the same time, it noted that "[t]he burden of prescriber certification has been minimized to the extent possible" because each provider need only provide one certification to each of the two drug sponsors for mifepristone. 2021 REMS 001574; *see also* 2021 REMS 001597.

2. Patient Agreement Form. FDA similarly concluded that the single-page Patient Agreement Form, which "ensures that patients are informed of the risks of

serious complications associated with" use of mifepristone for this indication, "does not impose an unreasonable burden on providers or patients" and "remains necessary to assure the safe use of Mifepristone." 2021 REMS 001574, 1578; *see also* 2021 REMS 001597. FDA explained that "literature that focused on the informed consent process" "d[id] not provide evidence that would support removing" the Patient Agreement Form requirement. 2021 REMS 001576, 1577; *see also* 2021 REMS 001597. Specifically, the agency found "no publications which directly addressed" the Patient Agreement Form. 2021 REMS 001576. Moreover, seven studies focusing on the informed consent process contained "no outcome data" or "other evidence demonstrating that informed consent made the Patient Agreement Form unnecessary." 2021 REMS 001576-1577.

Further, as with prescriber certification, FDA found that the potentially significant increase in the number of medical abortion providers weighed in favor of retaining the Patient Agreement Form. 2021 REMS 001597; *see also* 2021 REMS 001578. The agency noted the "continued need to ensure that patients are consistently provided patient education under the Mifepristone REMS Program regarding the use and risks of mifepristone." 2021 REMS 001597; *see also* 2021 REMS 001575, 1578. The Patient Agreement Form, FDA explained, fulfills that need by "standardizing the medication information that prescribers communicate to their patients, including new prescribers." 2021 REMS 001597; *see also* 2021 REMS 001575, 1578. It also provides that information in a "brief and understandable format," thus minimizing the burden of this requirement. 2021 REMS 001578.

3. Pharmacy certification. FDA determined that the benefits of mifepristone for medical termination of early pregnancy would continue to outweigh the risks if the in-person dispensing requirement was removed, provided all other requirements of the REMS were met and a pharmacy certification requirement was added. 2021 REMS 001599; *see also* 2021 REMS 001600-1601. The pharmacy certification requirement permits pharmacies to dispense mifepristone upon prescription by a certified prescriber if the pharmacies become certified. 2021 REMS 001600-1601. FDA explained that, with the removal of the in-person dispensing requirement, the pharmacy certification requirement is necessary to ensure that pharmacies are aware of and agree to follow applicable REMS requirements and that only prescriptions from certified prescribers are filled. 2021 REMS 001601.

B. Plaintiffs fail to identify any relevant statutory factor that FDA did not reasonably consider

1. Plaintiffs disagree with how FDA weighed the § 355-1(g)(4)(B) considerations, but they fail to identify any way in which FDA's consideration was unreasonable. Congress assigned FDA the responsibility to determine the conditions under which drugs are safe. 21 U.S.C. § 355(d). Based on the evidence, FDA concluded that the evidence remains insufficient to find that mifepristone would be safe without the requirements for the prescriber certification, the Patient Agreement Form, and pharmacy certification. That determination is entitled to the utmost deference. *Balt. Gas & Elec., Co.*, 462 U.S. at 103; *Schering Corp.*, 51 F.3d at 399; *see also Am. Coll. Of Obstetricians & Gynecologists*, 141 S. Ct. at 579 (Roberts, C.J., concurring in the grant of

application stay) (explaining that the "significant deference" owed to FDA's judgments weighed against "compel[ling] the FDA to alter the regimen for medical abortion").

First, Plaintiffs seemingly dispute that it is necessary for prescribers to have the qualifications that the prescriber certification requirement calls for. Pl. MSJ 32. They base this argument on the assertion that no "proven link" has been shown demonstrating that specific risks identified in the mifepristone labeling were "caused by mifepristone." *Id*. But this ignores the fact that "a causal relationship need not have been definitively established" for a warning to appear on a drug's labeling. 21 C.F.R. § 201.57(c)(6). Similarly, FDA's rationale for requiring prescriber certification did not rely on whether or not mifepristone has "caused" serious complications; it was that mifepristone prescribers must be prepared to "detect[]" and "manage[]" the "serious and potentially fatal complications associated with medical abortion" (even though rarely occurring). 2021 REMS 001573. This reasonably ensures women will receive necessary treatment if they experience, for example, a "missed ectopic pregnancy" or "heavy bleeding from incomplete abortion." *Id*.[7] Thus, it was plainly within FDA's authority to find this requirement necessary to "mitigate a specific serious risk listed in the labeling of the drug." 21 U.S.C. § 355-1(f).

[7] Plaintiffs state that, unlike "serious and sometimes fatal infections or bleeding," "missed ectopic pregnancies are not one of the two serious risks listed on the mifepristone label." Pl. MSJ 32 n.8. Although missed ectopic pregnancy does not appear in the labeling's boxed warning, the labeling does identify ectopic pregnancy as a contraindication, 2023 SUPP 1490, 1493, and includes warnings concerning it, 2023 SUPP 1495, 1497; *see also* 2021 REMS 001574 (discussing risks posed by ectopic pregnancy). FDA agrees that mifepristone does not cause missed ectopic pregnancies.

Plaintiffs further argue that the requirement is unnecessary because prescribers may possess those qualifications without so certifying. Pl. MSJ 32. But FDA did not rest its decision solely on the need for prescribers to have these qualifications. FDA also invoked (1) the absence of new evidence demonstrating a reason to depart from the agency's earlier determination that prescriber certification was necessary to ensure the safe use of mifepristone, (2) the prescriber certification's role in ensuring that patient deaths are reported to FDA, and (3) the potential for a significant increase in the number of prescribers following elimination of the in-person dispensing requirement. 2021 REMS 001573-1574; *see also* 2021 REMS 001597. Given these considerations, it was reasonable for FDA to find that the evidence did not support eliminating this requirement.

More broadly, Plaintiffs fault FDA for its "demand for safety data" showing that the drug would be safe if the prescriber certification requirement were eliminated. Pl. MSJ 33. But under § 355-1(g)(4)(B), FDA determines if an existing REMS should be modified to, among other things, "ensure the benefits of the drug outweigh the risks of the drug." Absent evidence establishing safe use without this requirement, it was reasonable for FDA to decline to eliminate it, particularly when it determined that the burden of prescriber certification "has been minimized to the extent possible by requiring prescribers to certify only one time for each [sponsor]." 2021 REMS 001574; *see also* 2021 REMS 001597.

Second, Plaintiffs argue that the Patient Agreement Form should be eliminated because informed consent provides sufficient protection for patients and because the

information in the Patient Agreement Form is also contained in the Medication Guide provided to patients. Pl. MSJ 34. But FDA considered the relevant evidence and rejected this argument. 2021 REMS 001576, 1577; *see also* 2021 REMS 001597. Plucking one sentence from the agency's rationale out of context, Plaintiffs assert that FDA has no authority to require ETASU with a purpose of "standardizing the medication information on the use of mifepristone that prescribers communicate to their patients." Pl. MSJ 34; 2021 REMS 001578. But standardizing the information patients receive about a drug can be an important part of ensuring the drug's safety, and thus FDA is well within its authority in considering that fact when imposing an ETASU "to mitigate [] risk" by including "documentation of safe-use conditions." 21 U.S.C. § 355-1(f)(3)(D); *see* 2021 REMS 001578 (explaining that the Patient Agreement Form helps "ensure[] that each provider, including new providers, informs each patient of the appropriate use of mifepristone, risks associated with treatment, and what to do if the patient experiences symptoms that may require emergency care").

Plaintiffs next take issue (Pl. MSJ 34) with FDA's view that the "potential doubling of medical abortion providers supports the continued need" for the Patient Agreement Form. 2021 REMS 001597. Plaintiffs argue that FDA had previously acknowledged that it has "removed REMS requirements in other [drug] programs based on the integration of the REMS safe use condition into clinical practice," and there are always some "new providers" of a drug. FDA 465; Pl. MSJ 34. This quotation was taken from a 2016 memorandum recommending the removal of the Patient Agreement

Form[8] while also recommending that the in-person dispensing requirement *be retained*. In 2021, the potential doubling of providers upon the *removal* of in-person dispensing provided additional support for continuing to require the Patient Agreement Form under the specific circumstances present here. This is consistent with the broader fact that, as explained below, the Agency considers REMS on a case-by-case basis and did so here.

Third, Plaintiffs assert that there is no "statutory basis" for the pharmacy certification requirement. Pl. MSJ 35. That is plainly wrong: the REMS statute specifically contemplates such a requirement. *See* 21 U.S.C. § 355-1(f)(3)(B) ("The [ETASU] . . . may require that . . . pharmacies . . . that dispense the drug are specially certified[.]"). And while Plaintiffs dispute the justification for the prescriber certification requirement, they do not seriously dispute that, given FDA's decision to retain that requirement, the pharmacy certification requirement was necessary to ensure that it continues to be met.

Plaintiffs observe that FDA did not require pharmacy certification for mail-order pharmacies in the period during the COVID-19 public health emergency in which the agency was exercising enforcement discretion for the in-person dispensing requirement, and there were no increased adverse events reported during that period. Pl. MSJ. 35. But this argument overlooks the difference between an agency's temporary exercise of enforcement discretion in a public health emergency, and its subsequent decision to

[8] The Patient Agreement Form was ultimately retained in the 2016 REMS decision, *see* FDA 685-69, and again in the decision challenged here.

permanently remove the in-person dispensing requirement as part of a REMS modification. When making the latter decision, FDA reasonably exercised its statutory authority to require pharmacy certification to ensure (among other things) that prescriber certification continues to be followed.

2. Plaintiffs also err by emphasizing the factors in 21 U.S.C. § 355-1(a)(1) that they claim FDA failed to consider. Pl. MSJ 1, 4, 25-27, 28, 29. As its title ("Initial Approval") suggests, § 355-1(a)(1) governs FDA's decision to require an applicant seeking *initial approval* of a new drug for a particular use to propose a REMS. 21 U.S.C. § 355-1(a)(1). It provides that FDA may require the applicant to propose a REMS if the agency determines that one is "necessary to ensure that the benefits of the drug outweigh the risks of the drug." *Id.* In making that determination, FDA must consider certain specific factors. These factors do not apply here.

Notably, Plaintiffs are not challenging FDA's "initial approval" of the mifepristone REMS. 21 U.S.C. § 355-1(a)(1). Instead, they challenge only the January 2023 REMS modification, a decision governed by § 355-1(g). As discussed above, § 355-1(g)(4)(B) sets out distinct considerations relevant to an agency decision to require modifications to a REMS. Moreover, it does not cross-reference or incorporate the factors enumerated in § 355-1(a)(1). Indeed, § 355-1 recognizes an initial determination under subsection (a)(1) as distinct from a later determination to modify the REMS under subsection (g). *See* 21 U.S.C. § 355-1(h)(1) (distinguishing between a "proposed [REMS] for a drug submitted under subsection (a)" and a "proposed modification to an approved [REMS] for a drug submitted under subsection (g)"); *id.* § 355-1(h)(3), (4)

(establishing different dispute resolution procedures for decisions under subsections (a)(1) and (g)).

Nor would it make sense to apply the § 355-1(a)(1) factors to a REMS modification decision. Several of those factors are directed at drugs that have not yet been marketed for a particular use subject to a REMS. *See, e.g.*, *id.* § 355-1(a)(1)(A) ("*estimated* size of the population *likely* to use the drug") (emphasis added); *id.* § 355-1(a)(1)(B) ("seriousness of the disease or condition that is *to be treated* with the drug") (emphasis added); *id.* § 355-1(a)(1)(C) ("*expected* benefit of the drug") (emphasis added); *id.* § 355-1(a)(1)(E) (referring to "the population *likely* to use the drug") (emphasis added); *id.* § 355-1(a)(1)(F) ("*new* molecular entity") (emphasis added). If Congress intended to require FDA to apply the § 355-1(a)(1) factors when assessing drugs already marketed subject to a REMS, it would have used language more amenable to that assessment.

3. Plaintiffs also argue that FDA failed to apply the factors in § 355-1(f)(1)-(3), which governs FDA's decision whether to require a REMS to include ETASU. Pl. MSJ 1, 2, 4, 25-27, 31, 32, 34, 35. But subsection (f), like subsection (g), looks to whether ETASU are "necessary to assure safe use of the drug" and are not unduly burdensome. *See id.* § 355-1(f)(1), (2); *accord id.* § 355-1(g)(4)(B)(i) and (ii); *see also id.* § 355-1(f)(1)(A) (permitting FDA to require elements to assure safe use if the drug "can be approved only if, or would be withdrawn unless, such elements are required"). And here, FDA weighed precisely those factors. As discussed, based on its review of the evidence, FDA concluded that (1) there was insufficient evidence to demonstrate that mifepristone

would continue to have a favorable safety profile if the prescriber certification requirement or the Patient Agreement Form were eliminated, but (2) there was sufficient evidence supporting removal of the in-person dispensing requirement, provided that all other REMS requirements were met and a pharmacy certification requirement was added.

Plaintiffs claim that the § 355-1(f)(1)(A) ETASU standard is "more demanding" than the REMS standard and that FDA failed to apply it. Pl. MSJ 25-26, 32, 35. But their argument boils down to little more than faulting the agency for not saying the right "magic" words. FDA found that the ETASU were "*necessary* to assure the safe use of Mifepristone," 2023 SUPP 1376-78, and "*necessary* to ensure the benefits of [mifepristone] outweigh the risks," 2023 SUPP 1397, 1421-22; drugs that FDA finds to be "unsafe" under their conditions of use must be withdrawn, *see* 21 U.S.C. § 355(e); *Mut. Pharm. Co. v. Bartlett*, 570 U.S. 472, 476 (2013) (noting that approval requires that a drug's "'probable therapeutic benefits must outweigh its risk of harm'").[9]

Plaintiffs argue that FDA failed to reasonably account for burdens on access, *see, e.g.*, Pl. MSJ 31, but Plaintiffs do not explain how any of the ETASU could have been modified in a way to make them less burdensome while ensuring the drug's safety. While Plaintiffs contend that FDA should have eliminated the ETASU entirely, that approach is inconsistent with FDA's determination that prescriber certification, the

[9] *See also* https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/frequently-asked-questions-about-cder ("No drug product is 'perfectly' safe. . . . For every drug FDA approves, the benefits are balanced against its risks.").

Patient Agreement Form, and pharmacy certification are *necessary* for safety. 2021 REMS 001574, 1597, 1599, 1600-1601, 001803-1807, 1808-1811.

Misreading § 355-1(f)(2)(D)(i), Plaintiffs fault FDA for not specifically comparing mifepristone to a diverse array of other drugs. Pl. MSJ 10, 23-24, 35; Compl. ¶ 121. But the statute does not require FDA to undertake such an apples-to-oranges comparison. Several of the drugs that Plaintiffs mention are over-the-counter drugs with vastly different conditions of use, indications, and risks. And opioids are controlled substances that are subject to other regulatory regimes that may affect the healthcare delivery system and patient access.[10] There is no basis in the statute for requiring FDA to use these different drugs as a template for the regulation of mifepristone.

Plaintiffs fault FDA for requiring a REMS for Mifeprex and its generic when FDA did not require a REMS for Korlym (a different drug product with mifepristone as its active ingredient, *see supra* n.1). Pl. MSJ 23-24. In deciding whether to require a REMS for a particular drug, FDA makes a case-by-case determination that involves weighing the drug's risks and benefits in light of its particular conditions of use and other factors. *See* 21 U.S.C. § 355-1(a)(1). Indeed, FDA conducted this case-by-case inquiry for Korlym, explicitly considering the REMS for Mifeprex. FDA explained why Korlym does not require a REMS to assure safe use of the drug to treat Cushing's syndrome. Among other things, FDA noted that women with Cushing's syndrome are "unlikely to be

[10] For example, § 1263 of the Consolidated Appropriations Act of 2023 requires opioid prescribers to complete training. Pub. L. 117-328, § 1263, 136 Stat. 4459, 5683 (Dec. 29, 2022). Plaintiffs fail to account for this in noting that FDA's Opioid Analgesic REMS does not contain a prescriber certification requirement. Pl. Mem. 4.

pregnant" due to the underlying disease, and that the sponsor voluntarily distributes Korlym exclusively through specialty pharmacies. FDA 298, 304; *see generally* FDA 292-306. Because Mifeprex and its generic (on the one hand) and Korlym (on the other) have different approved conditions of use—and different benefits and risks in light of those uses—FDA was not compelled to treat the drugs as the same.

4. In any event, even if Plaintiffs were right that FDA did not fully consider particular statutory factors relevant to REMS modification, any such error would be harmless. *See* 5 U.S.C. § 706. Here, FDA determined that the REMS with ETASU is necessary to assure mifepristone's safe use. Because FDA cannot approve a drug for use under conditions that the agency has not determined are safe, 21 U.S.C. § 355(d), none of the factors Plaintiffs identify could have changed the agency's conclusion.

C. FDA considered all relevant evidence

Plaintiffs' attack on FDA's consideration of the evidence likewise fails. Pl. MSJ 28-31. As explained above, FDA reviewed evidence from a wide variety of sources, including "advocacy groups," "healthcare providers and researchers," and the *Purcell* Plaintiffs. FDA did not ignore relevant evidence.

1. As noted, published literature was only one of several types of information that FDA considered. With respect to that literature, the agency's decision to focus on objective safety data when considering whether the evidence supported modifying the REMS with regard to the prescriber certification and in-person dispensing requirements was plainly reasonable. To determine whether to modify an existing REMS, FDA must assess whether the evidence before it shows that the drug would remain safe with the

contemplated modification. Objective safety data, which here included, among other things, data regarding safety outcomes during the period in which in-person dispensing was not being enforced, was the evidence most relevant to these modifications, and Plaintiffs do not contend otherwise.

Plaintiffs misunderstand the import of FDA's focus on such evidence. They contend that FDA "excluded statements by prominent medical professional societies," Pl. MSJ 28, "refused to consider" qualitative studies and healthcare professional narratives, Pl. MSJ 30, and "excluded all '[d]ata on the logistics of accessing abortion care,'" Pl. MSJ 31. But FDA considered all relevant evidence before it. *See supra* pp. 19-20. The agency generally focused on "objective safety data" because that was the kind of evidence most germane to its safety analysis. The APA's requirement that an agency consider all relevant evidence before it does not oblige it to agree that any particular type of evidence should be given weight in its determination.

Here, context makes plain that FDA's statements that it "excluded" certain types of evidence meant only that it concluded that such evidence did not bear on evaluation of some of the modifications it was considering. 2021 REMS 001604-1608. Indeed, "Appendix A" to FDA's 2021 REMS review memorandum contains a chart that lists the references that FDA "excluded" from the review. The chart describes the contents of the listed references and briefly notes the reason that FDA did not give the item weight in making its determination. 2021 REMS 001604-1608. The very existence of the chart belies Plaintiffs' contention that FDA did not "consider" the references in the APA sense.

Nor are Plaintiffs correct that FDA refused to consider anything but objective safety data. The 2021 REMS review memorandum makes equally clear that FDA did not "categorically" refuse to consider qualitative data, such as practice guidelines and data from practitioner surveys regarding provider volume. To the contrary, FDA reviewed and considered practice guidelines and survey data in evaluating the Patient Agreement Form ETASU because of the relevance of the practice guidelines, the quality of the survey data, and the relevance of likely changes in provider volume. 2021 REMS 001572, 1577.

2. The only evidence Plaintiffs point to (Pl. MSJ 29) that FDA did not consider is the Canadian study referenced above. *See supra* pp. 17-18. But, as noted, that study was not published until 2022—*after* FDA completed its 2021 REMS review and directed the sponsors of mifepristone to propose a modified REMS. FDA reasonably imposed a cut-off date of July 2021 for its systematic review of the literature. 2021 REMS 001570. Indeed, had FDA declined to establish a cut-off date, it would never have completed its review. *See Ferguson v. Dep't of Educ.*, No. 09-cv-10057-FM, 2011 WL 4089880, at *10 (S.D.N.Y. Sept. 13, 2011) (finding it reasonable" for agency "to restrict the temporal scope" of inquiry to avoid "'never-ending process.'") (quoting *Coven v. OPM*, No. 07-cv-1831-PHX-RCB, 2009 WL 3174423, at *7 (D. Ariz. Sept. 29, 2009)).

Perhaps Plaintiffs mean to suggest that FDA was required to review any evidence published before the actual *approval* of the proposed modification. But that would open the door to the same "never-ending process." The statute provides that a sponsor has 120 days or a "reasonable time[]" to propose a modified REMS after being

directed to do so. 21 U.S.C. § 355-1(g)(4)(B). FDA then generally has 180 days to act on that proposal. *Id.* § 355-1(h)(2)(A). If the agency had to reevaluate its decision to request a modification every time a new, potentially relevant study is published in that long gap and notify the sponsor to amend its pending request for modification based on that study, the evaluation would never be completed. In any event, FDA was never asked to consider the Canadian study in connection with the January 2023 REMS modification. *See supra* pp. 17-18.

IV. Plaintiffs' Constitutional Claims Fail

Finally, Defendants are entitled to summary judgment on Counts III and IV of the Complaint, which invoke the equal protection component of the Fifth Amendment's Due Process Clause. Plaintiffs' claims are subject to rational-basis review. *Dobbs v. Jackson Women's Health Org.*, 597 U.S. 215, 300 (2022). The Court must therefore reject Plaintiffs' constitutional claims if the January 2023 REMS modification is "rationally related to a legitimate [government] interest." *Giarrantano v. Johnson*, 521 F.3d 298, 302-03 (4th Cir. 2008). The government has a legitimate interest in protecting public health. *Antunes v. Rector & Visitors of Univ. of Va.,* 627 F. Supp. 3 553, 564 (W.D. Va. 2022). For the reasons explained above, FDA's decision to approve modification but not elimination of the Mifepristone REMS Program is rationally related to that interest. Therefore, FDA is entitled to summary judgment on Plaintiffs' constitutional claims.

V. If Necessary, The Parties Should Brief The Issue Of Remedy Separately

The Court should grant Defendants' motion for summary judgment and deny Plaintiffs' motion for summary judgment. However, if the Court determines that

Plaintiffs' motion should be granted, Defendants respectfully request the opportunity to brief the appropriate remedy. Defendants note that, while Plaintiffs' motion requests that the Court "either vacate the 2023 Mifepristone REMS or remand it to FDA,"[11] ECF No. 68, at 2, they do not explain which they believe is the appropriate remedy. In Defendants' view, for example, even if the Court finds for Plaintiffs on the merits, it would not be appropriate to vacate any agency action.

CONCLUSION

For the foregoing reasons, the Court should grant Defendants' cross-motion for summary judgment and deny Plaintiffs' motion for summary judgment.

December 18, 2024

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[11] By contrast, the *Washington* plaintiffs have requested remand without vacatur because they correctly recognize that vacating the January 2023 REM would have "disruptive consequences." Plaintiff States' Motion for Summary Judgment, *Washington, et al. v. FDA, et al.*, 23-cv-3026-TOR, ECF No. 156, at 25. The *Purcell* (formerly *Chelius*) plaintiffs similarly have not requested vacatur. Plaintiffs' Motion for Summary Judgment, *Purcell, et al. v. Becerra, et al.*, 17-cv-00493-JAO-RT, ECF No. 221, at 3-5 (seeking only declaratory relief and remand).

CERTIFICATE OF SERVICE

I hereby certify that, on December 18, 2024, I electronically filed the foregoing with the Clerk of the Court using the CM/ECF system, which will send notification of such filing to all counsel of record.

/s/ Noah T. Katzen
NOAH T. KATZEN